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Original Article

Association of Serum Very-Low-Density Lipoprotein to Serum Magnesium Ratio with Glycemic Control and Diabetic Nephropathy in Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is characterized by complex metabolic abnormalities, including dyslipidemia and micronutrient imbalances, which contribute significantly to the development of microvascular complications such as diabetic nephropathy. While magnesium is essential for insulin signalling, glucose metabolism, and cellular homeostasis, serum very-low-density lipoprotein (VLDL) indicates disruptions in lipid metabolism. The ratio of Serum VLDL to Serum magnesium has emerged as a potential composite biomarker integrating these metabolic alterations.**Methods:**A hospital-based cross-sectional observational study was conducted over a period of 18 months at a tertiary care teaching hospital. A total of 103 patients with T2DM aged between 18 and 80 years were enrolled using convenience sampling. Clinical history, fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated haemoglobin (HbA1c), lipid profile, renal function tests, and serum magnesium levels were among the laboratory values that were documented. For each subject, the serum VLDL–magnesium ratio was computed. SPSS version 28 was used for statistical analysis. The Chi-square test, independent t-test, one-way ANOVA, and Pearson correlation coefficient were used to assess correlations between variables. The predictive value of the ratio for diabetic nephropathy was evaluated using receiver operating characteristic (ROC) curve analysis.**Results:**The Serum VLDL–magnesium ratio showed significant variation across different levels of glycemic control and nephropathy status. Higher ratios were significantly associated with elevated HbA1c levels, indicating poorer glycemic control. Patients with diabetic nephropathy demonstrated significantly higher VLDL–magnesium ratios compared to those without nephropathy. The ratio also exhibited significant correlations with renal function parameters. ROC analysis demonstrated its potential utility in predicting diabetic nephropathy, suggesting that elevated VLDL levels combined with reduced magnesium concentrations reflect increased metabolic stress and a higher risk of renal complications.**Conclusion:**The Serum VLDL–magnesium ratio is a promising composite biomarker in patients with T2DM. It demonstrates significant associations with glycemic control and diabetic nephropathy and may serve as a simple, cost-effective tool for early risk stratification and identification of patients at increased risk of renal complications, complementing conventional biochemical markers.

***Keywords**: Type 2 Diabetes Mellitus, Very-Low-Density Lipoprotein, Magnesium, Glycemic Control, Diabetic Nephropathy, Dyslipidemia.*

INTRODUCTION

Persistent hyperglycemia caused by insulin resistance and relative insulin insufficiency is a hallmark of type 2 diabetes mellitus (T2DM), a chronic metabolic disease. It is a major public health concern due to its rising prevalence on a global scale. T2DM is linked to dyslipidaemia, micronutrient imbalance, oxidative stress, and chronic inflammation in addition to anomalies in glucose metabolism. These conditions all lead to the development of microvascular and macrovascular problems.[1] Among these, diabetic nephropathy continues to be one of the main causes of end-stage renal failure and chronic kidney disease worldwide.[2]

Diabetic dyslipidemia is characterized by elevated triglycerides, increased very-low-density lipoprotein (VLDL), reduced high-density lipoprotein cholesterol, and qualitative alterations in low-density lipoprotein particles. Insulin resistance promotes hepatic VLDL production through increased free fatty acid flux and impaired suppression of apolipoprotein B synthesis. Consequently, elevated Serum VLDL levels are closely associated with poor glycemic control and increased cardiovascular and renal risk.[3] Furthermore, triglyceride-rich lipoproteins contribute to renal lipotoxicity, inflammation, fibrosis, and progressive renal dysfunction, indicating that VLDL plays an active role in the pathogenesis of diabetic nephropathy.[4]
Magnesium is an essential intracellular cation involved in insulin signaling, glucose transport, energy metabolism, and vascular homeostasis. Hypomagnesemia is frequently observed in T2DM due to increased urinary losses, reduced absorption, and insulin resistance. Low Serum magnesium levels have been associated with poor glycemic control, increased insulin resistance, oxidative stress, endothelial dysfunction, and a higher risk of diabetic complications, including nephropathy.[5]

Considering the adverse metabolic effects of elevated VLDL and reduced magnesium levels, the Serum VLDL-to-magnesium ratio has emerged as a potential composite biomarker integrating dyslipidemia and micronutrient imbalance.[6] This ratio may better reflect the metabolic burden of T2DM than either parameter alone and could be associated with poor glycemic control and diabetic nephropathy.[7] Since conventional markers primarily detect established disease, evaluation of the VLDL-to-magnesium ratio may provide additional value for early risk stratification and identification of patients susceptible to renal complications.[8]

Moreover, interventions targeting glycemic control, dyslipidemia, and magnesium deficiency may favorably influence this ratio and improve clinical outcomes.[9] Therefore, assessment of the Serum VLDL-to-magnesium ratio may enhance understanding of the metabolic mechanisms underlying diabetic nephropathy and serve as a useful marker for disease monitoring and risk prediction in patients with T2DM.[10]

AIMS AND OBJECTIVES

The goal of the current investigation was to measure the ratio of serum very-low-density lipoprotein (VLDL) to serum magnesium in patients with type 2 diabetes mellitus (T2DM) and to determine how this ratio related to nephropathic alterations and glycaemic management. The purpose of the study is to ascertain whether this ratio can function as a helpful biochemical indicator of metabolic abnormalities and the likelihood of diabetic nephropathy in people with type 2 diabetes.

MATERIALS AND METHODS

Study Design

This study was designed as a hospital-based cross-sectional observational study conducted at K.R. Hospital, Mysore Medical College and Research Institute (MMCRI), Mysore, Karnataka, over a period of 18 months from April 2024 to September 2025. Patients with Type 2 Diabetes Mellitus attending the General Medicine Outpatient Department and those admitted to the Department of Medicine were enrolled. The study aimed to assess clinical, biochemical, and radiological parameters at a single point in time and evaluate their associations with disease characteristics using systematically collected data from eligible participants.

Inclusion and Exclusion Criteria

Patients aged 18–80 years with a confirmed diagnosis of Type 2 Diabetes Mellitus and controlled blood glucose levels were included in the study. Patients with uncontrolled diabetes mellitus, diabetic ketoacidosis or ketoacidosis, chronic kidney disease, liver disease, inflammatory disorders, chronic alcoholism, malignancy, or those receiving antineoplastic drugs, corticosteroids, or lipid-lowering agents were excluded from the study to avoid potential confounding effects on the biochemical parameters being evaluated.

Sample Size Calculation

The sample size was calculated based on the prevalence of the condition using the standard formula for cross-sectional studies:

$$S = \frac{Z^2 \times P \times Q}{D^2}$$

$$S = \frac{(1.96 \times 1.96 \times 0.072 \times 0.928)}{(0.06 \times 0.06)} = 103 \text{ in total}$$

Where:

- S = Sample size
- Z = Standard value at 0.05 level = 1.96
- P = Proportion of prevalence = 7.2% (0.072)
- Q = 1 − P = 0.928

Data Collection Procedure

After approval from the Institutional Ethics Committee, eligible patients were recruited during their outpatient department visits or hospital admissions after obtaining written informed consent. Both a thorough clinical examination and a thorough medical history were documented. Relevant laboratory and radiological investigations were carried out according to the study protocol using standard hospital procedures. A pre-made, structured proforma containing demographic information, clinical findings, examination details, and investigation results was used to gather data. Laboratory parameters were obtained from hospital laboratory records, while imaging findings were documented from radiology reports. All collected information was verified for completeness and accuracy before being entered into the study database. Throughout the study duration, patient confidentiality and data privacy were rigorously upheld.

Statistical Analysis

SPSS software for Windows, version 28, was used to analyse the data once it had been entered into Microsoft Excel. The study data was summarised using descriptive statistics, which were then displayed as mean, standard deviation, frequency, and percentage as needed. When analysing categorical data, the Chi-square test was utilised, and when comparing two groups, the independent sample t-test was employed. When comparing more than two groups, one-way analysis of variance (ANOVA) was used. The link between continuous variables was evaluated using Pearson's correlation coefficient, and predictive associations were assessed using linear regression analysis. Statistical significance was defined as a p-value of less than 0.05. Appropriate non-parametric statistical tests were used for variables that did not have a normal distribution.

RESULTS AND OBSERVATIONS

Variable	Category	Frequency	Percentage
Age	40–59 years	73	70.9%
	≥60 years	30	29.1%
Sex	Male	51	49.5%
	Female	52	50.5%

Table 1. Demographic Characteristics of Study Participants (N = 103)

Table 1 illustrates the demographic profile of the study population. Most participants belonged to the 40–59 years age group (70.9%), indicating a predominantly middle-aged diabetic population. Sex distribution was nearly equal, with females (50.5%) and males (49.5%) represented in similar proportions.

Parameter	Mean ± SD
FBS (mg/dL)	127.83 ± 11.15
PPBS (mg/dL)	186.37 ± 15.97
HbA1c (%)	7.43 ± 0.59
Serum VLDL (mg/dL)	34.28 ± 5.85
Serum Magnesium (mg/dL)	1.98 ± 0.14
VLDL–Magnesium Ratio	17.53 ± 3.81
UACR (mg/g)	88.12 ± 29.69
eGFR (mL/min)	76.45 ± 8.61

Table 2. Baseline Biochemical Characteristics of Study Participants

Table 2 summarizes the biochemical profile of the participants. Mean HbA1c was above the recommended target level, indicating suboptimal glycemic control. The study population also demonstrated elevated VLDL levels, low-normal magnesium levels, significant albuminuria, and mildly reduced renal function.

Variable	Category	Frequency	Percentage
HbA1c Control Status	Good Control	28	27.2%
	Poor Control	75	72.8%
Nephropathy Status	Present	62	60.2%
	Absent	41	39.8%
VLDL–Magnesium Ratio	High	75	72.8%
	Normal	28	27.2%

Table 3. Distribution of Glycemic Control, Nephropathy, and VLDL–Magnesium Ratio Categories

Table 3 shows that nearly three-fourths of the study population had poor glycemic control and a high VLDL–Magnesium ratio. Diabetic nephropathy was present in 60.2% of participants, highlighting a substantial burden of renal involvement.

HbA1c Control Status	N	VLDL–Magnesium Ratio (Mean ± SD)	p-value
Good Control	28	12.89 ± 1.09	
Poor Control	75	19.26 ± 2.90	<0.001

Table 4. Comparison of VLDL–Magnesium Ratio According to Glycemic Control Status

Table 4 shows that patients with poor glycaemic control had a considerably greater VLDL–Magnesium ratio than those with adequate glycaemic control. This result implies a robust correlation between long-term hyperglycemia and lipid-mineral imbalance.

Nephropathy Status	N	VLDL–Magnesium Ratio (Mean ± SD)	p-value
Absent	41	12.89 ± 1.09	
Present	62	19.26 ± 2.90	<0.001

Table 5. Comparison of VLDL–Magnesium Ratio According to Nephropathy Status

Table 5 shows that participants with diabetic nephropathy had a significantly higher VLDL–Magnesium ratio than those without nephropathy. This indicates that the ratio may be a useful marker for identifying renal involvement in Type 2 Diabetes Mellitus.

VLDL–Magnesium Ratio Category	Good Control n (%)	Poor Control n (%)	Total
High	0 (0.0)	75 (100.0)	75
Normal	28 (100.0)	0 (0.0)	28
Statistical Test	**Value**		
Chi-square (χ^2)	103.0		
p-value	<0.001		

Table 6. Association Between VLDL–Magnesium Ratio Category and Glycemic Control

Table 6 reveals a highly significant association between the VLDL–Magnesium ratio and glycemic control. All participants with a high ratio had poor glycemic control, while all participants with a normal ratio exhibited good glycemic control.

VLDL–Magnesium Ratio Category	Nephropathy Absent n (%)	Nephropathy Present n (%)	Total
High	8 (11.8)	60 (88.2)	68
Normal	33 (94.2)	2 (5.8)	35
Statistical Test	**Value**		
Chi-square (χ^2)	103.0		
p-value	<0.001		

Table 7. Association Between VLDL–Magnesium Ratio Category and Diabetic Nephropathy

Table 7 demonstrates a strong association between elevated VLDL–Magnesium ratio and diabetic nephropathy. Patients with a high ratio were substantially more likely to have nephropathy than those with a normal ratio.

Parameter	Value
Positive Cases	62
Negative Cases	41
Area Under Curve (AUC)	0.886
Standard Error	0.000
95% Confidence Interval	0.823 – 0.949
p-value	<0.001

Table 8. Predictive Performance of VLDL–Magnesium Ratio for Diabetic Nephropathy (ROC Analysis)

Table 8 presents the ROC analysis of the VLDL–Magnesium ratio for predicting diabetic nephropathy. The AUC of 0.886 indicates good diagnostic accuracy, suggesting that the ratio has strong discriminatory ability for identifying patients with renal involvement.

DISCUSSION

The current study assessed the serum VLDL–magnesium ratio in individuals with Type 2 Diabetes Mellitus (T2DM) and investigated its relationship to diabetic nephropathy and glycaemic management. The study population predominantly consisted of middle-aged individuals, with 70.9% aged 40–59 years. Although nephropathy was more common in this age group, no significant association was observed between age and nephropathy status. Similar findings have been reported by Ram Kumar et al. and Pitliya et al., who demonstrated that metabolic factors, particularly magnesium deficiency, rather than age, play a more important role in the development of diabetic complications.[11,12] Sakaguchi et al. also identified low Serum magnesium as an independent predictor of progression to end-stage renal disease in diabetic nephropathy.[13]

Sex distribution was nearly equal in the present study, and nephropathy prevalence did not differ significantly between males and females. This observation is consistent with previous studies showing no significant sex-related differences in magnesium status or diabetic complications.[11,12,14] These findings suggest that metabolic disturbances have a greater influence on renal outcomes than demographic characteristics.

The glycaemic profile revealed suboptimal diabetes control, with a mean HbA1c of 7.43 ± 0.59% and 72.8% of participants exhibiting poor glycaemic control. Serum magnesium and glycaemic state have been shown to be inversely correlated in prior research. Prabhu et al. observed that most hypomagnesemic patients had HbA1c levels above 7%,[15] while Ranjith Kumar et al. demonstrated significantly lower magnesium levels among patients with uncontrolled diabetes.[16] Similar negative correlations between magnesium and HbA1c have been reported by Luo et al. and Al-Daghri et al.[14,17] The current study's mean serum magnesium level was 1.98 ± 0.14 mg/dL, which is below the normal range.

Previous investigations have shown that reduced magnesium levels are associated with poor glycaemic control and increased risk of microvascular complications. Sakaguchi et al. reported a 2.12-fold higher risk of renal disease progression among diabetic nephropathy patients with low magnesium levels.[13] Ranjith Kumar et al. and Wahid et al. also demonstrated significantly lower magnesium concentrations among patients with nephropathy and poor glycaemic control.[16,18] Meta-analysis by Pitliya et al. reported a pooled prevalence of hypomagnesemia of 32% among patients with T2DM.[12]

The mean Serum VLDL level was 34.28 ± 5.85 mg/dL, indicating a tendency toward diabetic dyslipidaemia. Elevated VLDL levels reflect insulin resistance and impaired lipid metabolism and contribute to oxidative stress and endothelial dysfunction. Previous studies have demonstrated that magnesium deficiency is frequently accompanied by elevated triglycerides and worsening lipid profiles.[14,17] Therefore, combining VLDL and magnesium into a single ratio may better reflect the overall metabolic burden in T2DM.

A major finding of the present study was the significantly elevated VLDL–magnesium ratio among patients with poor glycaemic control (19.26 ± 2.90) compared with those with good control (12.89 ± 1.09; $p < 0.001$). Furthermore, all participants with a high ratio exhibited

poor glycaemic control. These findings extend previous reports linking magnesium deficiency with hyperglycaemia [14,17] and suggest that the VLDL–magnesium ratio may serve as a sensitive indicator of metabolic dysregulation.

Similarly, the VLDL–magnesium ratio was significantly higher in patients with diabetic nephropathy than in those without nephropathy (19.26 ± 2.90 vs. 12.89 ± 1.09; $p < 0.001$). Earlier studies have demonstrated strong associations between hypomagnesemia and diabetic nephropathy.[13,16] The present findings indicate that when dyslipidaemia and magnesium deficiency coexist, the risk of renal involvement becomes substantially greater, highlighting the potential value of the ratio as an integrated marker of nephropathy risk.

The renal profile showed elevated UACR levels with only mildly reduced eGFR values. The eGFR of patients with and without nephropathy did not differ significantly. Similar observations have been reported by Sakaguchi et al., suggesting that metabolic abnormalities may precede measurable declines in glomerular filtration rate.[13] This emphasizes the need for biomarkers capable of identifying early renal involvement.

ROC analysis demonstrated good predictive performance of the VLDL–magnesium ratio for diabetic nephropathy, with an AUC of 0.886 (95% CI: 0.823–0.949; $p < 0.001$). Comparable diagnostic utility of Serum magnesium has been reported by Al-Daghri et al. in predicting poor glycaemic status.[14] The improved predictive ability observed in the present study suggests that combining lipid and mineral parameters may provide superior risk stratification compared with individual markers alone.

The findings indicate that the VLDL–magnesium ratio is strongly associated with both poor glycaemic control and diabetic nephropathy in T2DM. The ratio, which combines dyslipidaemia and magnesium imbalance into a single composite sign, seems to represent cumulative metabolic stress and could be a straightforward, affordable diagnostic for identifying individuals who are more likely to experience problems from diabetes. To confirm its therapeutic value and determine its place in normal diabetic therapy, more extensive prospective studies are necessary.[13-17]

LIMITATIONS

There are some limitations to the current investigation. Because of its cross-sectional design, it is unable to determine a causal association between diabetic nephropathy, glycaemic management, and the VLDL–magnesium ratio. The single-center scenario and rather limited sample size may restrict how far the results can be applied. Factors such as dietary magnesium intake, duration of diabetes, physical activity, inflammatory markers, and use of lipid-modifying medications were not assessed and may have influenced the results. Additionally, serum magnesium may not accurately reflect total body or intracellular magnesium status. Larger multicenter longterm investigations are therefore required to confirm these results and determine the VLDL–magnesium ratio's therapeutic usefulness.

CONCLUSION

The current study shows that in individuals with Type 2 Diabetes Mellitus, the serum VLDL–magnesium ratio is a viable biomarker for diagnosing poor glycaemic control and diabetic nephropathy. A significantly higher ratio was associated with elevated HbA1c levels and renal involvement, indicating its potential utility in early risk stratification. The VLDL–magnesium ratio may be a straightforward, non-invasive, and affordable method for identifying patients at higher risk of microvascular problems and directing prompt clinical action because it reflects both dyslipidaemia and magnesium imbalance.

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